

*Letters to the Editor***Correspondence re: C.V. Rao, et al., Inhibition of 2-Amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine-induced Lymphoma Formation by Oltipraz. *Cancer Res.*, 56: 3395–3398, 1996****Letter**

In 1991, we observed and reported that oltipraz significantly inhibited the development of hematopoietic tumors of male F344 rats in an experiment designed to study the cancer chemopreventive effects of oltipraz against AFB<sub>1</sub><sup>1</sup> (1). The incidence of hematopoietic tumors was 53% in the rats receiving AFB<sub>1</sub> alone and was reduced to a 30% incidence in the AFB<sub>1</sub> group exposed concurrently to dietary oltipraz ( $P < 0.05$ ). We suggested that additional studies be undertaken of this wholly unexpected finding regarding oltipraz (1). It is indeed gratifying to see our observations corroborated and extended (2).

In our study, oltipraz was fed for only 4 weeks during the administration of AFB<sub>1</sub>; thereafter, the rats received no more AFB<sub>1</sub> or oltipraz (1). Aflatoxin B<sub>1</sub> is primarily an hepatic carcinogen and has not been associated with the initiation of hematopoietic tumors (3). The hematopoietic tumors in our rats were MCL, a common neoplasm of the F344 rat (4). We believe our results indicate that oltipraz blocked one or more early processes of MCL development. We did not have experimental groups that received oltipraz alone or a control group with no chemical treatment, so we cannot be sure that our result was not due to an interaction of AFB<sub>1</sub> and oltipraz.

Thymic lymphosarcomas (lymphomas) are malignant hematopoietic tumors known to be induced in rats by *N*-nitroso-*N*-propylurea (5, 6). In fact, the incidences and latencies of lymphomas in these studies are similar to those reported by Rao *et al.* (2) for 2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine. The lymphomas induced by *N*-nitroso-*N*-propylurea and 2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine are different tumors than MCL, and the observation of Rao *et al.* (2) is a significant addition to the knowledge in this field.

With two reports of oltipraz preventing hematopoietic tumors (1, 2) and the paucity of approaches to prevention of hematopoietic tumors, oltipraz may present a unique opportunity for chemoprevention in this setting.

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**References**

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**Reply**

We appreciate the comments of Dr. Roebuck and his associates (1) on our paper (2), and we concur that it is important to fully test the chemopreventive potential of oltipraz in hematopoietic tumors. We differ with regard to the comment “it is gratifying to see our observations corroborated and extended,” for several reasons. First of all, the study in 1991 by Roebuck *et al.* (3) was designed to investigate the chemopreventive effect of oltipraz on aflatoxin B<sub>1</sub>-induced liver cancer in male F344 rats. In that study, the investigators made the observation (from the pooled data of two different experimental groups) that 53% F344 rats given aflatoxin B<sub>1</sub> produced MCL<sup>1</sup> and about 30% incidence of MCL in oltipraz-fed rats. Unfortunately, there was no vehicle control. Vehicle controls are essential for any bioassay and are critically important in a F344 rat model because of the very high incidence of MCL (one of the most common neoplasms; about 30–40%) in these animals (4, 5). Also, the extended studies carried out by Coulombe (6) indicate that aflatoxin B<sub>1</sub> was not associated with hematopoietic tumors. However, on the basis of this information, it is not clear whether oltipraz significantly protects F344 rats from MCL (untreated control rats, 30–40% incidence, *versus* 30% incidence in oltipraz-treated rats) and/or whether aflatoxin B<sub>1</sub> is significantly induces of MCL. If so, it should be shown by using the proper vehicle control in animals free of MCL.

In contrast to the study by Roebuck *et al.* (3), our study (2) was designed to investigate the chemopreventive effect of oltipraz on PhIP-induced T-cell lymphomas, which are quite different from MCL. Unlike MCL, thymic lymphomas are not commonly found in F344 rats (4, 5). Also, our studies used proper experimental vehicle controls for both PhIP as well as oltipraz (2). Induction of thymic lymphomas by other synthetic carcinogens and limitations and disadvantages of such animal models have in fact been discussed in detail in our paper (Ref. 2, Introduction and Discussion).

In conclusion, whether our study corroborated or extended the findings by Roebuck *et al.* (3), we think that they afford a unique

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<sup>1</sup> The abbreviations used are: MCL, mononuclear cell leukemia; PhIP, 2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine.

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<sup>1</sup> The abbreviations used are: AFB<sub>1</sub>, aflatoxin B<sub>1</sub>; MCL, mononuclear cell leukemia.

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